UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/533,670	12/30/2005	Eswaran Krishnan Iyer	WH-3	6215

58478 7590 12/16/2008

BIO INTELLECTUAL PROPERTY SERVICES (BIO IPS) LLC
8509 KERNON CT.
LORTON, VA 22079

EXAMINER	
PURDY, KYLE A	

ART UNIT	PAPER NUMBER
1611	

MAIL DATE	DELIVERY MODE
12/16/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/533,670	IYER ET AL.	
	Examiner	Art Unit	
	Kyle Purdy	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-81* is/are pending in the application.

4a) Of the above claim(s) *14-72* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *73-81* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. The Examiner acknowledges receipt of the amendments filed on 10/20/2008 wherein claim 73 has been amended.

2. Claims 73-81 are presented for examination on the merits. Claims 14-72 remain withdrawn. The following rejections are made.

Response to Applicants' Arguments

3. Applicants arguments filed 10/20/2008 regarding the rejection of claims 73-81 made by the Examiner under 35 USC 103(a) over Whitcomb et al. (US 6011049) in view of Timmins et al. (WO 99/47128), Timmins et al. (US 6031004) and Antarker et al. (US 2006/0057202) have been fully considered and they are found persuasive. This rejection is **WITHDRAWN** as being overcome by amendment.

Objection, Claimed Subject Matter Not in Specification

4. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter of claim 73. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Claim 73 recites, 'the delivery system released around 30-50% of the slow release component within a period of about 2-3 hours and not less than 75% of the slow release component within a period of about 24 hours'. While the limitation is present in originally filed claim 12, since cancelled, there is no support within the specification for such limitations. Appropriate correction is required.

New Rejections, Necessitated by Amendment

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. **Claims 73-81 are rejected under 35 U.S.C. 103(a) as being unpatentable over Whitcomb et al. (US 6011049; of record) in view of Timmins et al. (WO 99/47128; of record), Timmins et al. (US 6031004; of record), Antarker et al. (US 20060057202; of record) and Tahara et al. (J. controlled Release, 1995, 35, 59-66).**

7. Whitcomb discloses a pharmaceutical combination for treating diabetes wherein the combination includes a glitazone, a biguanide and a sulfonylurea (see instant claim 73). It is taught that the therapeutic composition comprising these ingredients are especially useful for treating diabetes and associated complications such as cardiovascular disease and retinopathy. The mode by which the compounds are administered includes a single triple-combination dosage or administered individually (i.e. physically separated) as performed clinically, and exemplified dosage forms include tablets, capsules as wells controlled release formulations (see column 4, lines 35-40; see instant claim 73).

8. Whitcomb fails to teach however the biguanide as being a slow release component, the sulfonylurea as being either slow or immediate release and the glitazone as being immediate release. Additionally, Whitcomb fails to teach the slow release as releasing between around 30-50 of the component within a period of about 2-3 hours and not less than75% of the component within a period of 24 hours.

9. Timmins (herein '128) is directed to a biphasic controlled release delivery system for high solubility pharmaceuticals such as the biguanide, metformin. The composition comprises hydrophilic polymers (hydroxypropyl methylcellulose), hydrophobic polymers (ethylcellulose and microcrystalline cellullose) and hydrophobic materials (waxes and fatty alcohols) (see abstract and pages 17-18; see instant claims 73-76). Example 4 teaches a composition which comprises about 50% metformin (see instant claim 78) as well as possess a hydrophilic:hydrophobic polymer component at a ratio of 9:1 (see instant claim 77).

10. The teaching of Timmins (herein '004) is directed to salts of metformin. It is disclosed that salts of metformin are less soluble in water and provide an opportunity for formulating controlled release systems to achieve a desired release rate (see column 2, line 40). Example 8 for instance teaches a sustained release composition which comprises metformin and glipizide (a sulfonylurea) (see instant claim 73). It also comprises microcrystalline cellulose (hydrophobic polymer) and hydroxypropyl methylcellulose (hydrophilic polymer) at a weight ratio of about 1:2 (see instant claims 73, 74 and 77). The metformin is present at about 85% by weight of the composition (see instant claim 78) and the glipizide is present at about 0.7% by weight (see instant claim 79).

11. Antarkar is directed to multilayer tablets containing thiazolidinediones (i.e. glitazone) and optionally biguanides for immediate release (see abstract; see instant claim 73). In the compositions the glitazone can comprise from 5-50% of the compositions weight (see instant claim 80). Additionally, in Example 1 it is disclosed that microcrystalline cellulose and hydroxypropylmethylcellulose are used at a weight ratio of about 20:1 and Example 3 teaches a

sustained release composition for metformin wherein methacrylic acid (hydrophobic) and hydroxypropyl methylcellulose are used at a weight ratio of about 1:2.5 (see instant claim 77).

12. Tahara is directed to the mechanism behind sustained release tablets prepared with hydroxypropyl methylcellulose. It is taught that there are several factors which may influence the rate at which the drug is released from the sustained release matrix including drug concentration, infiltration rate of medium into the sustained release matrix, and erosion rate of the matrix system (see abstract). Several Figures are provided by Tahara illustrating the rate of release for various sustained release systems (see figures 4A and 5A). Figure 5A shows taht by using more viscous hydroxypropyl methylcellulose, a slower rate of release is provided whereas using less viscous hydroxylpropyl methylcellulose a quicker rate of release is provided. In fact, Figure 5A shows that at about 3 hours about 25% of the drug has been release and at 24 hours the drug has been completely released from the sustained release matrix (see instant claim 73).

13. It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Whitcomb with 128, 004, Antarkar and Tahara with a reasonable expectation for success in arriving at an oral delivery system comprising a slow release biguanide component, a slow or rapid release sulfonylurea component and an immediate release glitazone component. The teaching of Whitcomb specifically discloses the combiantion of these three classes of compounds as useful together for treating diabetes and stipulates for them to be formulated into sustained and rapid release composition. Whitcomb however does not set forth which components are to be sustained and immediately released nor does it set forth any specific details regarding the component amounts, the rate of sustained release or the presence of additional hydrophobic/hydrophilic excipients. 128 discloses a slow release

biguanide composition useful for the gastrointestinal release. It teaches that the composition can comprises a hydrophilic polymer, a hydrophobic polymer and a hydrophobic material. The teaching of 004 is directed to novel slow release compositions for biguanide and sulfonylureas. Timmins sets forth specific weight percentages for these two ingredients (see above) which obviate the instantly claimed amounts. Moreover, it also sets forth excipient requirements (see above) which obviate the instant claim requirements. Antarkar teaches compositions for the immediate release of glitazones. Its disclosure also obviates the instant claims limitations with respect to the glitazones weight percentage (see above) in the composition. With respect to the properties of the sustained release portion of the composition, it is obvious. According to Tahara, optimization of sustained release compositions is routinely undertaken in the art of sustained release formulations. It is that that infiltration rate of the medium into the matrix, the erosion rate of the system and the drug concentration all affect the release profile of the drug present in the sustained release matrix. Moreover, one would have been motivated to isolate each of these three factors and adjust them such that the final product would be one with optimized properties sufficient to enable the greatest pharmaceutical effect to the user of the composition. If such a result were that around 20-30% of the drug was released within 2-3 hours and by 24 more than 75% of the drug had been released, then this would be a product of ordinary skill and optimization, not one of innovation. As all of the features of the instant application are disclosed or suggested by the prior art and because there is a clear motivation to combine their features, one of ordinary skill in the art would have a reasonable expectation for success in combining the references above to arrive at the instantly claimed invention. Therefore, the invention as a whole

is *prima facie* obvious to one ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in absence of evidence to the contrary.

Conclusion

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kyle A. Purdy whose telephone number is 571-270-3504. The examiner can normally be reached from 9AM to 5PM.

15. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau, can be reached on 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

16. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Kyle Purdy/
Examiner, Art Unit 1611
December 11, 2008

/David J Blanchard/
Primary Examiner, Art Unit 1643